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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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1623	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ptopatentcommunication@lockelord.com

Office Action Summary	Application No.	Applicant(s)	
	10/567,114	ZHILOV ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71 and 82-110* is/are pending in the application.

4a) Of the above claim(s) *105,107 and 109* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71,81-104,106,108 and 110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3 pgs / 13 Jan 2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 13 Jan 2010, in which claim 71 is amended to change the scope and breadth of the claim, claims 72-81 are canceled, and new claims 82-110 are added.

The terminal disclaimer filed 13 Jan 2010 is acknowledged and discussed herein.

This application is the national stage entry of PCT/RU03/00346, filed 04 Aug 2003.

Claims 71 and 82-110 are pending in the current application. Claims 105, 107 and 109, drawn to non-elected inventions, are withdrawn. Claims 103 and 71, 81-102, 104, 106, 108 and 110 (in part) are examined on the merits herein.

Terminal Disclaimer

The terminal disclaimer filed on 13 Jan 2010 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on copending Application No. 10/567113 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Objections Withdrawn

Applicant's Amendment, filed 13 Jan 2010, with respect to objections to claim 72 has been fully considered and is persuasive, as claim 72 is canceled.

This objection has been **withdrawn**.

Rejections Withdrawn

Applicant's Amendment, filed 13 Jan 2010, with respect to objections to claim 71-73 and 76 and 77 rejected under 35 U.S.C. 112, first paragraph, as not being enabled for the full scope of the claim has been fully considered and is persuasive with regard to claims 72, 73, 76 and 77, as claim 72, 73, 76 and 77 are canceled.

This rejection of 72, 73, 76 and 77 has been **withdrawn**. The rejection of claim 71 is modified as recited below.

Applicant's Amendment, filed 13 Jan 2010, with respect to objections to claim 71-73 and 76 and 77 rejected under 35 U.S.C. 112, second paragraph, as being indefinite has been fully considered and is persuasive, as claim 72, 73, 76 and 77 are canceled and claim 71 is amended to recite a single mechanism of action.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 13 Jan 2010, with respect to objections to claim 71-73 and 76 and 77 rejected under 35 U.S.C. 102(b) as being anticipated by Minin et al. (US Patent 5,512,573, issued 30 Apr 1996, of record) has been fully considered and is

persuasive with regard to claims 72, 73, 76 and 77, as claim 72, 73, 76 and 77 are canceled.

This rejection of 72, 73, 76 and 77 has been **withdrawn**. The rejection of claim 71 is modified as recited below.

Applicant's Amendment, filed 13 Jan 2010, with respect to objections to claim 71-73 and 76 and 77 rejected under 35 U.S.C. 102(e) as being anticipated by Henry et al. (US Patent 6,953,799, filed 30 Oct 2002, of record) has been fully considered and is persuasive with regard to claims 72, 73, 76 and 77, as claim 72, 73, 76 and 77 are canceled.

This rejection of 72, 73, 76 and 77 has been **withdrawn**. The rejection of claim 71 is modified as recited below.

Applicant's terminal disclaimer filed on 13 Jan 2010 with respect to claims 71-73 and 76 and 77 are provisionally rejected on the ground of nonstatutory double patenting over claims 28-33 of copending Application No. 10/567113 has been fully considered and is persuasive, as claims 72, 73, 76 and 77 are canceled and the terminal disclaimer identifying copending Application No. 10/567113 has been reviewed and is accepted.

This provisional rejection has been **withdrawn**.

Election/Restrictions

Newly submitted claims 105, 107 and 109 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Applicant elected the invention of Group IX in the Response to Restriction filed on 23 Mar 2009 and newly submitted claim 105 corresponds the invention of Group VIII, newly submitted claim 107 corresponds the invention of Group X, and newly submitted claim 109 correspond the invention of Group XI, previously withdrawn.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 105, 107 and 109 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Further, claims 71, 81-102, 104, 106, 108 and 110 are examined according the elected invention of Group IX and the elected species as elected in the Response to Restriction filed on 23 Mar 2009.

Claim Objections

Claim 71, 85, 86, 88-90, 93, 95, 97 and 99-101 are objected to because of the following informalities:

- claims 71, 86, 90, 93, 95, 97, 99 and 101 recite the grammatical error "having biological activity like as activity of a compound of a purine system of a body", where it appears to mean having biological activity of a compound of a purine system;

- claims 71, 86, 90, 93 and 95 recite the grammatical error "nucleus and non-nucleus cells", where the noun "nucleus" appears to be used in place of the adjective "nucleated";
- claim 82 recites at line 3 "pancreatic," which appears to be a typographic omission of pancreatic diabetes recited in canceled claim 73;
- claim 85 recites at line 2 "insulin resistance,." where a period appears after the comma;
- claim 85 recites at line 2 "hyper fatty academia" as a typographical error of hyper fatty acidemia;
- claim 88 recites the grammatical error "ischemic diseases of heart";
- claim 89 recites the grammatical error "ischemic diseases of human brain";
- claim 100 recites the typographical or grammatical error "cholestasis icluding pregnants";
- claim 102 recites at line 2-3 the typographical or grammatical error "embolism after surgery with vessel".

Appropriate correction is required.

The following are modified grounds of rejection necessitated by Applicant's Amendment, filed 13 Jan 2010, in which claim 71 is amended to change the scope and breadth of the claim, claims 72-81 are canceled, and new claims 82-110 are added.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

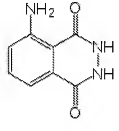
Amended Claims 71, 81-104, 106, 108 and 110 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for thymus involution and diseases known in the prior art such as acute hypoxia of myocardial infarct, insulin resistance, hyperglycemia, hyper fatty acidemia, hyperinsulemia, rheumatoid arthritis and amyotrophic lateral sclerosis, does not reasonably provide enablement for the full scope of the diseases treated in the claimed method such as the specific diseases recited in claims 82, 84, 85, 87, 89, 91, 92, 94, 96, 98, 100 and 102 not known in the prior art. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: A method for therapy of disease caused by intracellular acidosis, oxygen deficiency in a cell, excessively-formed free radicals, increasing the aggregation of thrombocytes and/or erythrocytes, or harmful action or disorders of nitrergic mechanisms of cell, said method comprising administering to a subject a pharmaceutically-effective amount of the elected species of sodium salt of 5-amino-benzo[d]-3H-pyridazine-1,4-dione.

The state of the prior art: Minin et al. (US Patent 5,512,573, issued 30 Apr 1996, of record) discloses the use of 5-aminophthaloylhydrazide and its salts administered in effective amounts as anti-hypoxic and defensive agents (abstract). The compound 5-aminophthaloylhydrazide or Luminol (column 1, lines 20-25), has the chemical structure



corresponding to the elected species. Minin et al. discloses the use of the sodium salt of 5-aminophthaloylhydrazide (column 4, lines 30-35). Minin et al. discloses the administration for the therapeutic effect of antioxidant action to treat acute hypoxia of myocardial infarct or heart attack (column 4, lines 50-55) and treatment of an excees of free oxygen radicals (column 4, ca. line 60). Minin et al. discloses that it is known that analogous drugs used for the same effect involve many complications and are not sufficiently effective (column 5, ca. line 55 and column 6, lines 5-10).

Henry et al. (US Patent 6,953,799, filed 30 Oct 2002, of record) discloses phthalazine compounds such as 5-amino-2,3-dihydro-1,4-phthalazinedione, also known

as luminol, (column 1, lines 45-50) administered to treat hosts with diseases involving impaired or aberrant intracellular redox states, which affects the membrane proton gradient, resulting in intracellular acidosis, and causes oxygen deficiency in cells and excessive formation of the free radical superoxide (column 2, lines 40-55). In the background section Henry et al. discloses luminol is known in the prior art to be useful in treating specific conditions such as "an inhibitor of poly (ADP-ribose) polymerase, an enzyme that responds to DNA damage (see U.S. Pat. Nos. 5,874,444; 5,719,151; 5,633,282), and to application in treating skin aging, Alzheimer's, atherosclerosis, osteoarthritis, osteoporosis, age-related macular degeneration, muscular dystrophy, immune senescence, viral infections, and cancer as diseases involving the functions of poly (ADP-ribose) polymerase (see U.S. Pat. Nos. 5,874,444; 5,719,151; 5,633,282)." Henry et al. teaches this therapy for treating, for example, atherosclerosis, burns, and chronic viral infections of the liver (column 4, lines 35-50), a hepatoprotective therapy. Henry et al. discloses it is known that said compound has an effect to treat the nitrergic mechanisms of cells in the central nervous system (column 10, lines 10-45). Henry et al. discloses said compound to treat insulin resistance, hyperglycemia, hyper fatty acidemia, hyperinsulemia, rheumatoid arthritis and amyotrophic lateral sclerosis (claim 1 at column 18, lines 20-30)

Long (The Essential Guide to Prescription Drugs, 1982, 3rd ed, p3-7, of record) teaches that it is well known in the art that there is an inescapable element of uncertainty that the desired effect of a drug will be exactly as intended or predicted (page 4, paragraph 2). Long teaches that one reason for this unpredictability is that a

drug is selected because its principal action is for the intended treatment will necessarily have multiple action which may render it not useful for the intended treatment (page 4, paragraph 3). Long teaches that another reason for this unpredictability is that all patients experience multiple responses to a drug and a body's reaction to a drug may vary widely from person to person (page 4, paragraph 4).

Frank et al. (Nat. Rev. Drug Discov., 2003, 2(7), p566-580, cited in PTO-892) drawn the use of clinical biomarkers in drug development and discovery (566, left column paragraphs 1-2 and right column, paragraphs 1-2). Frank et al. teaches that one of skill in the art understands that even if a drug candidate hits a drug target and alters a mechanism it does not necessarily affect the disease (page 568, figure 2 at top of page). Frank et al. suggests that extrapolation of mechanisms to clinical indications, or diseases, requires trials of common design and long-term follow up to in order ensure predictability for a particular mechanism and specific indication (page 569, left column, paragraph 2), implying the unpredictability of the extrapolation in the absence of such trials and long-term follow ups.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: The sheer number of possible diseases which are caused by the recited mechanisms and possible patient populations means that one skilled in the art cannot predict the usefulness for all possible methods for therapy of a disease encompassed within the instant invention. As recited above, Long teaches there is an inescapable element of uncertainty that the desired effect of a drug will be exactly as intended or predicted. Frank et al. suggests that extrapolation of

mechanisms to clinical indications, or diseases, requires trials of common design and long-term follow up in order to ensure predictability for a particular mechanism and specific indication. Therefore the claimed invention is unpredictable.

The Breadth of the claims: The scope of the claims is infinite. Any possible diseases which are caused by the recited mechanisms and possible patient populations could potentially be treated in the instant invention. Specific diseases and conditions are further recited in instant claims 82, 84, 85, 87, 89, 91, 92, 94, 96, 98, 100 and 102.

The amount of direction or guidance presented: The specification speaks generally about the role of homeostatic parameters in the survival and functioning of organisms, such as acid-base balance at page 1. It is suggested that the compound of the instant invention affects the pH within a cell (page 23). However, guidance is not given for the treatment of the full scope of the diseases encompassed within the instant method. It is suggested that the antiacidotic effect of dimephosphon is associated with regulating pneumonia at page 3, paragraph 34 of the instant PGPub. It is suggested for treating circulatory and tissue hypoxia, fever and peritonitis at page 1, paragraph 9. It is suggested for treatment of myocardial ischemia, or ischemic diseases of the heart, caused by endocellular acidosis at page 2, paragraph 26. Suggestion for treatment of the symptom of vomiting is found at page 1, paragraph 12. The working example of treatment of thymus involution is found at page 22, paragraph 257.

The presence or absence of working examples: The only working examples provided demonstrate the mechanism of action by *in vitro* effects on fibroblasts (page 24), *in vitro* effects on thrombocytes (page 32), *in vivo* antiaggregation of thrombocytes

(page 35 and page 40), and activity with regard to superoxide (page 50) and oxidative stress (page 52). However, the only working example of treatment of a disease is of thymus involution found at page 22, paragraph 257 of the instant PGPub. No working example is found for treatment of thrombosis, and the specification spanning page 15, paragraph 182 through page 17 paragraph 207 suggest the compounds do not influence the pathological effect on a normally functioning hemostasis system, having no effect on PATT (page 16, paragraph 191), prothrombin time index (page 17, paragraph 197) or autocoagulation activity (page 17, paragraph 203).

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable art such as treatment of a disease based on the mechanism of action based on using a drug selected because its principal action is for the intended treatment. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the invention with the full range of all possible diseases treat beyond those known in the art, (such as disclosed in Henry et al.) one skilled in the art would undertake a novel and extensive research program into the therapeutic effectiveness of the compound for all possible diseases caused by the recited mechanisms. Because this research would have to be exhaustive, and because it would involve such a wide and unpredictable scope of possible diseases, patient populations and treatment regimes, it would constitute an undue and unpredictable experimental burden.

> *Genentech*, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims, Applicants fail to provide information sufficient to practice the claimed invention for all possible diseases caused by the recited mechanisms for all patient populations beyond treatment of diseases known in the prior art and thymus involution.

Response to Applicant's Remarks:

Applicant's Remarks, filed 13 Jan 2010, have been fully considered and not found to be persuasive.

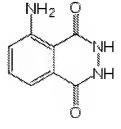
Applicant asserts that amended claim 71 reciting a method of treatment of diseases caused by intracellular acidosis (or reversible abnormal changes of pH of cells of the living body) is enabled by the specification. As recited above, Frank et al. (Nat. Rev. Drug Discov., 2003, 2(7), p566-580, cited in PTO-892) teaches that a drug candidate that hits a target and alters a mechanism does not necessarily affect a disease (page 568, figure 2 at top of page) and suggests that extrapolation of mechanisms to clinical indications, or diseases, requires trials of common design and long-term follow up to in order ensure predictability for a particular mechanism and specific indication (page 569, left column, paragraph 2), implying the unpredictability of the extrapolation in the absence of such trials and long-term follow ups. The level of unpredictability in the art in view of the lack of working examples is a critical factor to be considered, supporting the conclusion that it would constitute an undue and unpredictable experimental burden to practice the claimed invention for the full scope of the claim as discussed above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Amended Claims 71, 82, 86, 88, 90, 95-98, 101-104, 106, 108 and 110 are rejected under 35 U.S.C. 102(b) as being anticipated by Minin et al. (US Patent 5,512,573, issued 30 Apr 1996, of record).

Minin et al. discloses the use of 5-aminophthaloylhydrazide and its salts administered in effective amounts as anti-hypoxic and defensive agents (abstract). The compound 5-aminophthaloylhydrazide or Luminol (column 1, lines 20-25), has the chemical structure  corresponding to the elected species. Minin et al. discloses the use of the sodium salt of 5-aminophthaloylhydrazide (column 4, lines 30-35). Minin et al. discloses the administration for the therapeutic effect of antioxidant action to treat acute hypoxia of myocardial infarct or heart attack (column 4, lines 50-55

and column 7, lines 45-50), a form of arterial hypoxia and an ischemic disease of the heart, meeting limitations of instant claims 71, 82, 86, 88, 97 and 98. Minin et al. discloses the administration for treatment of an excess of free oxygen radicals (column 4, line 60), meeting limitations of instant claim 90. Minin et al. discloses the administration for the therapeutic effect of acute alterations in the blood stream to the brain (column 8, lines 45-55), or cerebral blood flow abnormalities, meeting limitations of instant claims 97, 98, 101 and 102. These diseases are necessarily caused by harmful action of chemical compounds action, such the action of chemical compounds in the deficiency of oxygen or the action of oxygen radicals, meeting limitations of instant claims 95 and 96.

Note that intracellular acidosis (or reversible abnormal changes of pH of cells of the living body) (claim 71), oxygen deficiency in cell (claim 86), increasing the aggregation of thrombocytes and erythrocytes (claim 97) or prophylaxis of decreasing the aggregation of thrombocytes and erythrocytes (instant claim 101) is merely considered to be new function or the unknown property or the mechanism of action of a treatment, 5-aminophthaloylhydrazide and its salts administered in effective amounts. It has been settled that the claiming of a new function or unknown property which is inherently present in the prior art method will not make the claim patentable as set forth in the 102(b) rejection above. Treatment of arterial hypoxia by administering the same compound is concluded to inherently act by the reversible abnormal changes of pH of cells of the living body based on the dependency of instant claim 82 from instant claim 71. Treatment of ischemic disease of the heart by administering the same compound

is concluded to inherently act by oxygen deficiency in cells based on the dependency of instant claim 88 from instant claim 86. Treatment of myocardial infarct by administering the same compound is concluded to inherently act by increasing the aggregation of thrombocytes and erythrocytes based on the dependency of instant claim 98 from instant claim 97. Treatment of cerebral blood flow abnormalities by administering the same compound is concluded to inherently act by increasing the aggregation of thrombocytes and erythrocytes or prophylaxis of decreasing the aggregation of thrombocytes and erythrocytes based on the dependency of instant claim 98 from instant claim 97 and instant claim 102 from instant claim 101.

That applicant may have determined a mechanism by which the active ingredient gives the pharmacological effect does not alter the fact that the compound has been previously used to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the encompassed within the instant method as claimed. Thus, the method steps in Minin et al. are the same as the method claimed herein. An explanation of why that effect occurs does not make novel or even unobvious the treatment of the conditions encompassed by the claims.

Moreover, the mechanism of action of a treatment does not have a bearing on the patentability of the invention if the method steps, i.e., administering the same compound in the same amount to the same or similar patient population, are already known even though Applicant has proposed or claimed the mechanism (e.g., intracellular acidosis (or reversible abnormal changes of pH of cells of the living body),

oxygen deficiency in cell, increasing the aggregation of thrombocytes and erythrocytes or prophylaxis of decreasing the aggregation of thrombocytes and erythrocytes). Applicant's recitation of a new mechanism of action for the prior art method will not, by itself, distinguish the instant claims over the prior art teaching the same or substantially identical method steps. Mere recognition of latent properties in the prior art does not render novel or nonobvious an otherwise known invention. See *In re Wiseman*, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. *In re Baxter Travenol Labs*, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Minin et al. is silent as to "said compound having the ability to normalize hydrogen ion concentration in cells to within physiologically-acceptable concentrations" or "having biological activity like as activity of a compound of a purine system of a body". However, this property of the compound is found to be an inherent property that is necessarily present from the chemical structure. "A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present", see MPEP 2112.01.

Response to Applicant's Remarks:

Applicant's Remarks, filed 13 Jan 2010, have been fully considered and not found to be persuasive.

Applicant notes that Minin et al. is silent as to the compound "having biological activity like as activity of a compound of a purine system of a body". However, as recited above, this property of the compound is found to be an inherent property that is necessarily present from the chemical structure.

Amended Claims 71, 82, 85, 86, 90, 93, 94-96, 99, 103, 104, 106, 108 and 110 are rejected under 35 U.S.C. 102(e) as being anticipated by Henry et al. (US Patent 6,953,799, filed 30 Oct 2002, of record).

Henry et al. discloses phthalazine compounds such as 5-amino-2,3-dihydro-1,4-phthalazinedione, also known as luminol, (column 1, lines 45-50) administered to treat hosts with diseases involving impaired or aberrant intracellular redox states, which affects the membrane proton gradient, resulting in intracellular acidosis, and causes oxygen deficiency in cells and excessive formation of the free radical superoxide (column 2, lines 40-55), meeting limitations of instant claims 71, 86 and 90. Henry et al. discloses said phthalazine compounds incorporated into pharmaceutical forms (column 2, lines 65-70 and column 3, lines 1-5), and discloses the sodium form of a phthalazine compound (column 17, lines 50-55), leading one of skill in the art to instantly envision the well-known pharmaceutically acceptable sodium salt. Henry et al. teaches this therapy for treating, for example, atherosclerosis, burns, and chronic viral infections of the liver (column 4, lines 35-50), a hepatoprotective therapy, meeting limitations of instant claim 99. Henry et al. discloses it is known that said compound has an effect to treat the nitrergic mechanisms of cells in the central nervous system (column 10, lines

10-45), meeting limitations of instant claim 93. Henry et al. discloses said compound to treat insulin resistance, hyperglycemia, hyper fatty acidemia, hyperinsulemia, rheumatoid arthritis and amyotrophic lateral sclerosis (claim 1 at column 18, lines 20-30), meeting limitations of instant claims 71, 82, 85, 93 and 94. These diseases are necessarily caused by chemical compounds action, such the action of chemical compounds in the deficiency of oxygen or the action of oxygen radicals, meeting limitations of instant claims 95 and 96.

Note that intracellular acidosis (or reversible abnormal changes of pH of cells of the living body) (claim 71), oxygen deficiency in cell (claim 86), excessively-formed free radicals (claim 90) is merely considered to be new function or the unknown property or the mechanism of action of a treatment, 5-aminophthaloylhydrazide and its salts administered in effective amounts. It has been settled that the claiming of a new function or unknown property which is inherently present in the prior art method will not make the claim patentable as set forth in the 102(e) rejection above. Henry et al. discloses the compound is known to operate by the claimed mechanisms of action. Treatment of insulin resistance, hyperglycemia, hyper fatty acidemia, hyperinsulemia and rheumatoid arthritis by administering the same compound is concluded to inherently act by the reversible abnormal changes of pH of cells of the living body based on the dependency of instant claim 82 from instant claim 71. Treatment of amyotrophic lateral sclerosis by administering the same compound is concluded to inherently act by the reversible nitrergic mechanisms of cells in the central nervous system based on the dependency of instant claim 94 from instant claim 93.

That applicant may have determined a mechanism by which the active ingredient gives the pharmacological effect does not alter the fact that the compound has been previously used to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the encompassed within the instant method as claimed. Thus, the method steps in Minin et al. are the same as the method claimed herein. An explanation of why that effect occurs does not make novel or even unobvious the treatment of the conditions encompassed by the claims.

Moreover, the mechanism of action of a treatment does not have a bearing on the patentability of the invention if the method steps, i.e., administering the same compound in the same amount to the same or similar patient population, are already known even though Applicant has proposed or claimed the mechanism (e.g., intracellular acidosis (or reversible abnormal changes of pH of cells of the living body), oxygen deficiency in cell, excessively-formed free radicals, disorders of nitrergic mechanisms of cell, harmful action or hepatoprotective action). Applicant's recitation of a new mechanism of action for the prior art method will not, by itself, distinguish the instant claims over the prior art teaching the same or substantially identical method steps. Mere recognition of latent properties in the prior art does not render novel or nonobvious an otherwise known invention. See *In re Wiseman*, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or

obviousness from, the prior art. *In re Baxter Travenol Labs*, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Henry et al. is silent as to "said compound having the ability to normalize hydrogen ion concentration in cells to within physiologically-acceptable concentrations" in terms of hydrogen ion concentration, however this property is implicit in the membrane proton gradient or "having biological activity like as activity of a compound of a purine system of a body". Further, this property of the compound is found to be an inherent property that is necessarily present from the chemical structure. "A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present", see MPEP 2112.01.

Response to Applicant's Remarks:

Applicant's Remarks, filed 13 Jan 2010, have been fully considered and not found to be persuasive.

Applicant notes that Henry et al. is silent as to the compound "having biological activity like as activity of a compound of a purine system of a body". However, as recited above, this property of the compound is found to be an inherent property that is necessarily present from the chemical structure.

The following are new grounds of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended Claims 82, 84, 85, 87, 89, 91, 92, 94, 96, 98, 100 and 102 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The claims recite specific diseases that are not described in the specification such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the now claimed invention as summarized by claim:

- 82. chronic pneumonia, pleurisy, obstructive bronchitis, anemias, pancreatic, febrile state, and rheumatoid arthritis.
- 84. radiation sickness.
- 85. insulin resistance, hyperglycemia, hyper fatty acidemia, and hyperinsulinemia.
- 87. bronchial asthma.
- 89. ischemic diseases of human brain.
- 91. chronic diffuse glomerulonephritis, sepsis, and cystic fibrosis.
- 92. tuberculosis.
- 94. amyotrophic lateral sclerosis and disseminated sclerosis, and cirrhosis.

- 96. diseases caused by chemical compounds action, toxic drug action as antibiotics, poisonings, and traumas.
- 98. cholelithiasis, inherited hemoglobinopathy, erythrocyte membranepathy, trombophlebiti, thrombosis, thrombocytosis, thrombocytopenia, cerebral blood flow abnormalities, instable angina, myocardial infarction, child's neural disorder, ischemic stroke, and migraine.
- 100. alcoholic intoxication, drug intoxication, persistent vomiting, hepatitis, hepatocirrhosis, infiltrative liver injury, hepatocellular carcinoma, cholestasis icluding pregnants, bile-duct obstruction, cholangitis, nutmeg liver, and cardiac cirrhosis.
- 102. cerebral blood flow abnormalities, embolism after surgery with vessel, ischemic stroke, and migraine.

Support for the antiacidotic effect of dimephosphon associated with regulating pneumonia is found at page 3, paragraph 34 of the instant PGPub, however no support is found for the subgenus of chronic pneumonia. Support for circulatory and tissue hypoxia, fever and peritonitis is found at page 1, paragraph 9. Support for treatment of myocardial ischemia, or ischemic diseases of the heart, caused by endocellular acidosis is found at page 2, paragraph 26. Support for treatment of thymus involution is found at page 22, paragraph 257. Support for the symptom of vomiting is found at page 1, paragraph 12, however no support is found for the subgenus of persistent vomiting. No support is found for treatment of thrombosis, however the specification spanning page

15, paragraph 182 through page 17 paragraph 207 suggest the compounds do not influence the pathological effect on a normally functioning hemostasis system, having no effect on PATT (page 16, paragraph 191), prothrombin time index (page 17, paragraph 197) or autocoagulation activity (page 17, paragraph 203).

While certain specific diseases appear in the amended claims filed 23 Mar 2009, for example at claim 73, upon further review of the specification at the time the application was filed these diseases are not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Amended Claims 71, 81-104, 106, 108 and 110 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Amended claims 71, 86, 90, 93, 95, 97, 99 and 101 recite "wherein said biologically active compound is a cyclic bioisostere of derivatives of a purine system having the general structural formula..." (emphasis added) Claim 103 recites "the cyclic bioisostere is a derivative of benzo[d]-3H-pyridazine-1,4-dione, having a general formula ..." (emphasis added) Claims 81-85, 87-89, 91, 92, 94, 96, 98, 100, 102-104, 106, 108 and 110 depend from claims 71, 86, 90, 93, 95, 97, 99 and 101 and incorporate all limitations therein. The language renders the claims indefinite because it

is unclear whether the modifier "cyclic bioisostere" is interpreted as separate from the phrase "derivatives of a purine system having the general structural formula..." or whether the phrase is a single concepts such that the recited general structural formula defines the "cyclic bioisostere of derivatives of a purine system". One of skill in the art would not be readily apprised of the metes and bounds of the claim because it is unclear if the method requires the administration of the compound having the general structural formula or if the method encompasses all cyclic bioisosteres of the compound having said general structural formula.

Conclusion

No claim is found to be allowable.

This Office Action details new grounds of rejection not necessitated by Applicant's Amendment. Accordingly, this Office Action is Non-Final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Eric S Olson/
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